In the Specification:

Please amend the specification as shown.

Please amend the paragraph on page 1, line 12, to page 3, line 7, as follows:

This invention relates to oligonucleotides (e.g. containing LNA) that are complementary to the human thioredoxin (TRX) putative oncogene, which has been found to modulate tumor cell growth and apoptosis inhibition in a variety of human cancers. TRX has also been closely linked with drug resistance in cancer treatments (Yokomizo et al. 1995. *Cancer Res.* 55:4293-4296; Kahlos et al. 2001.*Int.J.Cancer* 20;95:198-204). T.C. Laurent first described TRX in 1964 from *Escherichia Coli.* It is a ubiquitous and relatively conserved approximately 12 kDa oxireductant enzyme found in both prokaryotes and eukaryots (Holmgren. 1989. J.Biol.Chem. 264:13963-13966). TRX contains a dithiol disulfide active site which is involved in redox reactions through the formation of reversible disulfide bonds and which undergoes reversible thiol reduction by the NADPH-dependant enzyme thioredoxin reductase. The active site is highly conserved and contains a Cys-Gly-Pro-Cys sequence (SEQ ID NO: 149) (Holmgren 1985. Annu.Rev.Biochem. 54:237-71.:237-271). Mammalian thioredoxin family comprises TRX-1 and TRX-2. The first is the cytosolic and nuclear form and the later is the mitochondrial form. TRX-1 is the most extensively described and is a 104 amino acid protein that has been suggested to be represented in several mutated forms in the cell (Powis, et al.. 2001.Annu.Rev.Biophys.Biomol.Struct. 30:421-55.:421-455). Human TRX /TRX-1 (11.5-kDa) which is also known as Adult T-cell Leukaemia-derived Factor (ADF) (Gasdaska et al. 1994. Biochim.Biophys.Acta 1218:292-296) or Eosinophil cytotoxicity stimulating factor (Silberstein, et al. 1993. J.Biol.Chem. 268:9138-9142) has 5 cysteine residues which is 3 more than found in bacteria. These extra cysteines are responsible for the unique properties of human TRX (Gasdaska et al. 1994. Biochim.Biophys.Acta 1218:292-296). It has been shown that TRX modulates the DNA binding of transcription factors by redox control and hereby regulate gene transcription. Transcription factors described to be under TRX control are NF-κB (Matthews, et al. 1992. Nucleic Acids Res. 20:3821-3830), TFIIIC (Cromlish et al. J.Biol.Chem. 264:18100-18109), BZLF1(Bannister et al. 1991. Oncogene 6:1243-1250), p53

(Ueno, et al 1999. J.Biol.Chem. 274:35809-35815), the glucocorticoid receptor (Grippo, et al. 1983. J.Biol.Chem. 258:13658-13664) and indirectly AP-1 (Fos/Jun heterodimer)) (Abate et al. 1990. Science 249:1157-1161). TRX also increases DNA binding of AP-2, the estrogen receptor and PEBP2/CBF (Powis, et al.. 2001.Annu.Rev.Biophys.Biomol.Struct. 30:421-55.:421-455). Hypoxia-inducible factor 1 alpha (HIF-1α) has been shown to increase upon TRX elevation (Welsh et al. 2002. Cancer Res. 62:5089-5095), which could potentiate TRX as a anti-tumor-angiogenisis target. Furthermore it is involved in catalysing the conversion of nucleotides to deoxynucleotides, the first step in DNA synthesis that is essential for proliferation. TRX can serve as a signal for cancer cell growth probably by enhancing the autocrine activity of growth factors (Gasdaska et al. 1995. Cell Growth Differ. 6:1643-1650). It has been suggested that TRX up-regulates the alpha subunit of the high affinity IL-2 receptor in HTLV-1 transformed T-cells (Schenk et al. 1996. J.Immunol. 156:765-771) where IL-2 might be enhanced up to 1000 fold (Powis, et al.. 2001.Annu.Rev.Biophys.Biomol.Struct. 30:421-55.:421-455). TRX also increases cytokines like IL-1, IL-6, IL-8 and TNF-α (Schenk et al. 1996. J.Immunol. 156:765-771), thus influencing on immunologic disorders e.g. human rheumatoid arthritis. Stresses (e.g. hypoxia, lipopolysaccharide, O_2, hydrogen peroxide, phorbol ester, viral infection and infectious agents, X-ray radiation and UV irradiation, hormones and chemicals) induce TRX (Powis, et al.. 2001.Annu.Rev.Biophys.Biomol.Struct. 30:421-55.:421-455). The promoter region of the gene encoding TRX contains a series of stress responsive elements (Taniguchi et al. 1996. Nucleic Acids Res. 24:2746-2752). TRX-1 has been found over-expressed in a number of human primary tumors, and cancer cells secrete TRX-1 by a leaderless secretory pathway through an ER- Golgi independent manner (Rubartelli et al. 1992. J.Biol.Chem. 267:24161-24164). Human TRX has been suggested to be a potential target for anti-apoptosis and anti-proliferative treatment in various cancers as well as it may play a role in a variety of human disorders (Powis, et al.. 2001.Annu.Rev.Biophys.Biomol.Struct. 30:421-55.:421-455). Apoptosis has been inhibited through over-expression of TRX both in vitro and in vivo (Baker et al. 1997. Cancer Res. 57:5162-5167). Recombinant human TRX stimulates proliferation of normal cells and cultured cancer cells from a variety of solid tumors

(Gasdaska et al. 1995. Cell Growth Differ. 6:1643-1650.; Oblong et al. . J.Biol.Chem. 269:11714-11720) and TRX mRNA has been found to be over-expressed in human tumor cells. Redox inactive TRX on the other hand does not stimulate cell proliferation (Oblong et al. . J.Biol.Chem. 269:11714-11720). Surprisingly it has been found that malignancies of certain human primary tumor cells either express or over-express TRX compared to normal tissue. Examples are found within Gastric carcinoma (Grogan et al. 2000. Hum.Pathol. 31:475-481), malignant pleural mesothelioma (Kahlos et al. 2001.Int.J.Cancer 20;95:198-204), non-small cell lung carcinoma (Soini, et al. Clin.Cancer Res. 7:1750-1757), carcinoma of liver (Nakamura et al. Cancer 69:2091-2097), uterine cervix (Fujii et al.Cancer 68:1583-1591), pancreas cancer (Nakamura et al. Cancer Detect.Prev. 24:53-60), Colon cancer, Non-Hodgkin's lymphoma, Acute lymphocytic leukaemia and myeloma (Powis, et al.. 2001.Annu.Rev.Biophys.Biomol.Struct. 30:421-55.:421-455).

Please amend the paragraph on page 14, lines 6-16, as follows:

In another embodiment of the invention, said nucleosides are linked to each other by means of a phosphorothioate group. An interesting embodiment of the invention is directed to compounds of SEQ NO 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, and 57 wherein each linkage group within each compound is a phosphorothioate group. Such modifications is denoted by the subscript S. Alternatively stated, one aspect of the invention is directed to compounds of SEQ NO ~~5_A, 6_S, 7_S, 8_S, 9_A, 10_A, 11_A, 12_A, 13_A, 14_A, 15_A, 16_A, 17_A, 18_A, 19_A, 20_A, 21_A, 22_A, 23_A, 24_A, 25_A, 26_A, 27_A, 28_A, 29_A, 30_A, 31_A, 32_A, 33_A, 34_A, 35_A, 36_A, 37_S, 38_A, 39_A, 40_A, 41_A, 42_A, 43_A, 44_A, 45_A, 46_A, 47_A, 48_A, 49_A, 50_A, 51_A, 52_A, 53_A, 54_A, 55_A, 56_A and 57_A.~~ 68, 71, 74, 77, 80, 83, 86, 89, 92, 95, 98, 101, 104, 107, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, and 148.

Please amend the paragraph on page 14, lines 18-21, as follows:

A further aspect of the invention is directed to compounds of SEQ NO ~~5_B, 6_S, 7_S, 8_B, 9_B, 10_B, 11_B, 12_B, 13_B, 14_B, 15_B, 16_B, 17_B, 18_B, 19_B, 20_B, 21_B, 22_B, 23_B, 24_B, 25_B, 26_B, 27_B, 28_B, 29_B, 30_B, 31_B, 32_B, 33_B, 34_B, 35_B, 36_B, 37_S, 38_B, 39_B, 40_B, 41_B, 42_B, 43_B, 44_B, 45_B, 46_B, 47_B, 48_B, 49_B, 50_B, 51_B, 52_B, 53_B, 54_B, 55_B, 56_B, and 57_B.~~ 69, 72, 75, 78, 81, 84, 87, 90, 93, 96, 99, 102, 105, and 108.

Please amend the paragraph on page 14, lines 23-26, as follows:

A further aspect of the invention is directed to compounds of SEQ NO ~~5_C, 6_S, 7_S, 8_C, 9_C, 10_C, 11_C, 12_C, 13_C, 14_C, 15_C, 16_C, 17_C, 18_C, 19_C, 20_C, 21_C, 22_C, 23_C, 24_C, 25_C, 26_C, 27_C, 28_C, 29_C, 30_C, 31_C, 32_C, 33_C, 34_C, 35_C, 36_C, 37_S, 38_C, 39_C, 40_C, 41_C, 42_C, 43_C, 44_C, 45_C, 46_C, 47_C, 48_C, 49_C, 50_C, 51_C, 52_C, 53_C, 54_C, 55_C, 56_C, and 57_C.~~ 70, 73, 76, 79, 82, 85, 88, 91, 94, 97, 100, 103, 106, and 109.

Please amend the paragraph on page 46, lines 2-9, as follows:

First strand synthesis was performed using OmniScript Reverse Transcriptase kit (cat# 205113, Qiagen) according to the manufacturers instructions.

For each sample 0.5 μg total RNA was adjusted to 12 μl each with RNase free H_2O and mixed with 2 μl poly $(dT)_{12-18}$ (SEQ ID NO: 150) (2.5 μg/ml) (Life Technologies, GibcoBRL, Roskilde, DK), 2 μl dNTP mix (5 mM each dNTP), 2 μl 10x Buffer RT, 1 μl RNAguard™Rnase INHIBITOR (33.3U/ml), (cat# 27-0816-01, Amersham Pharmacia Biotech, Hørsholm, DK) and 1 μl OmniScript Reverse Transcriptase (4 U/μl) followed by incubation at 37°C for 60 minutes and heat inactivation of the enzyme at 93°C for 5 minutes.

Please amend the paragraph on page 47, lines 5-9, as follows:

For human TRX the PCR primers were:
forward primer: 5' aagcctttctttcattccctctc 3' (SEQ ID NO: 58) (final concentration in the assay; 0.3 μM)
reverse primer: 5' cttcttaaaaaactggaatgttggc 3' (final concentration in the assay; 0.3 μM) (SEQ ID NO: 59) and the PCR probe was: 5' FAM- gatgtggatgactgtcaggatgttgcttc-TAMRA 3' (SEQ ID NO: 60) (final concentration in the assay; 0.1 μM)

Please amend the paragraph on page 47, lines 18-22, as follows:

For quantification of mouse GAPDH mRNA the following primers and probes were designed: Sense primer 5'aaggctgtgggcaaggtcatc 3' (SEQ ID NO: 61) (0.3 μM final concentration),
antisense primer 5' gtcagatccacgacggacacatt (SEQ ID NO: 62) (0.6 μM final concentration),
TaqMan probe 5' FAM-gaagctcactggcatggcatggccttccgtgtt c-TAMRA 3' (SEQ ID NO: 63) (0.2 μM final concentration).

Please amend the paragraph on page 48, lines 2-11, as follows:

Northern blot analysis was carried out by procedures well known in the art essentially as described in Current Protocols in Molecular Biology, John Wiley & Sons.
The hybridisation probe was obtained by PCR-amplification of a TRX bp fragment from TRX cDNA obtained by reverse transcription PCR as described in example 8. The reaction was carried out using primers 5' ggatccatttccatcggtcc 3' (forward) (SEQ ID NO: 64) and 5' gcagatggcaactggttatgtct 3' (reverse) (SEQ ID NO: 65) at 0,5 μM final concentration each, 200

nM each dNTP, 1,5 mM $MgCl_2$ and Platinum Taq DNA polymerase (Invitrogen cat. no. 10966-018).

The DNA was amplified for 40 cycles on a Perkin Elmer 9700 thermocycler using the following program: 94°C for 2 min. then 40 cycles of 94°C for 30 sec. and 72°C for 30 sec. with a decrease of 0.5°C per cycle followed by 72°C for 7 min.

Please amend the paragraph on page 48, line 24, to page 49, line 4, as follows:

Samples of 1-5 µg of total RNA purified as described in example 7 were denatured and size separated on a 2,2 M formaldehyde/MOPS agarose gel.

RNA was transferred to positively charged nylon membrane by downward capillary transfer using the TurboBlotter (Schleicher & Schuell) and the RNA was immobilised to the membrane by UV crosslinking using a Stratagene crosslinker.

The membrane was prehybridised in ExpressHyb Hybridization Solution (Clontech cat. No. 8015-1) at 60°C and the probe was subsequently added for hybridisation. Hybridisation was carried out at 60°C and the blot was washed with low stringency wash buffer (2 x SSC, 0,1% SDS) at room temperature and with high stringency wash buffer (0,1 x SSC, 0,1% SDS) at 50°C.

The blot was exposed to Kodak storage phosphor screens and scanned in a BioRAD FX molecular imager. TRX mRNA levels were quantified by Quantity One software (BioRAD) Equality of RNA sample loading was assessed by stripping the blot in 0,5% SDS in H_2O at 85°C and reprobing with a labelled GAPDH (glyceraldehyde-3-phosphate dehydrogenase) probe obtained essentially as described above using the primers 5' aac gga ttt ggt cgt att 3' (forward) (SEQ ID NO: 66) and 5' taa gca gtt ggt ggt gca 3' (reverse) (SEQ ID NO: 67).

Please amend Table 2 on pages 51-54, as follows:

Table 2 Oligomeric compounds of the invention

Oligomeric compounds were evaluated for their potential to knockdown TRX mRNA in 15PC3 cells. The data are presented as percentage downregulation relative to mock transfected cells. Transcript steady state was monitored by Real-time PCR and normalised to the GAPDH transcript steady state. Note that all LNA C are 5'-Methyl-Cytosine.

SEQ ID NO	Positions (complementary)	Oligomeric compound Sequence 5'-3'	~~Seq ID + Desing~~ SEQ ID NO: & Internal NO	Specific design of Oligomeric compound Capital letters β-D-oxy-LNA S= phosphorthioate O= -O-P(O)$_2$-O- Small letters DNA sugar	% Inhibition at 25 nM oligo
5	14/1	TCCAAAGCACCAAACA	~~5A~~ 68 CUR2672	$T_sC_sC_sA_sa_sa_sg_sc_sa_sc_sc_sa_sA_sA_sC_sA$	72
			~~5B~~ 69	$T_sC_sC_sA_sa_sa_sg_sc_sa_sc_sc_sa_sA_sA_sC_sa$	
			~~5C~~ 70	$T_OC_OC_OA_Oa_sa_sg_sc_sa_sc_sc_sa_sA_OA_OC_OA$	
6	33/1	AAGGACCGATGGAAAT	~~6A~~ 71 CUR2673	$A_sA_sG_sG_sa_sc_sc_sg_sa_st_sg_sg_sA_sA_sA_sT$	68
			~~6B~~ 72	$A_sA_sG_sG_sa_sc_sc_sg_sa_st_sg_sg_sA_sA_sA_st$	
			~~6C~~ 73	$A_OA_OG_OG_Oa_sc_sc_sg_sa_st_sg_sg_sA_OA_OA_OT$	
7	206/1	TTTTCAGAGAGGGAAT	~~7A~~ 74 CUR2674	$T_sT_sT_sT_sc_sa_sg_sa_sg_sa_sg_sg_sG_sA_sA_sT$	49
			~~7B~~ 75	$T_sT_sT_sT_sc_sa_sg_sa_sg_sa_sg_sg_sG_sA_sA_st$	
			~~7C~~ 76	$T_OT_OT_OT_Oc_sa_sg_sa_sg_sa_sg_sg_sG_OA_O$	

				A_OT	
8	229/1	CAAGGAATATCAC GTT	~~8A~~ 77 CUR267 5	$C_sA_sA_sG_sg_sa_sa_st_sa_st_sc_sa_sC_sG_sT_sT$	>95
			~~8B~~ 78 CUR276 6	$C_sA_sA_sG_sg_sa_sa_st_sa_st_sc_sa_sC_sG_sT_st$	93
			~~8C~~ 79	$C_OA_OA_OG_Og_sa_sa_st_sa_st_sc_sa_sC_OG_O$ T_OT	
9	281/2	TGGAATGTTGGCG TGC	~~9A~~ 80 CUR267 6	$T_sG_sG_sA_sa_st_sg_st_st_sg_sg_sc_sG_sT_sG_sC$	>95
			~~9B~~ 81	$T_sG_sG_sA_sa_st_sg_st_st_sg_sg_sc_sG_sT_sG_sc$	
			~~9C~~ 82	$T_OG_OG_OA_Oa_st_sg_st_st_sg_sg_sc_sG_OT_O$ G_OC	
10	347/1	TCCTTATTGGCTCC AG	~~10A~~ 83 CUR267 7	$T_sC_sC_sT_st_sa_st_st_sg_sg_sc_st_sC_sC_sA_sG$	84
			~~10B~~ 84	$T_sC_sC_sT_st_sa_st_st_sg_sg_sc_st_sC_sC_sA_sg$	
			~~10C~~ 85	$T_OC_OC_OT_Ot_sa_st_st_sg_sg_sc_st_sC_OC_OA$ $_OG$	
11	73/1	GCTTCACCATCTT GGC	~~11A~~ 86 CUR267 8	$G_sC_sT_sT_sc_sa_sc_sc_sa_st_sc_st_sT_sG_sG_sC$	31
			~~11B~~ 87	$G_sC_sT_sT_sc_sa_sc_sc_sa_st_sc_st_sT_sG_sG_sc$	
			~~11C~~ 88	$G_OC_OT_OT_Oc_sa_sc_sc_sa_st_sc_st_sT_OG_O$ G_OC	

12	46/1	GACGAGCGGCTGTAAG	~~12A~~ 89 CUR2679	$G_sA_sC_sG_sa_sg_sc_sg_sg_sc_st_sg_sT_sA_sA_sG$	74
			~~12B~~ 90	$G_sA_sC_sG_sa_sg_sc_sg_sg_sc_st_sg_sT_sA_sA_sg$	
			~~12C~~ 91	$G_OA_OC_OG_Oa_sg_sc_sg_sg_sc_st_sg_sT_OA_OA_OG$	
13	167/1	CAAGGCCCACACCACG	~~13A~~ 92 CUR2680	$C_sA_sA_sG_sg_sc_sc_sc_sa_sc_sa_sc_sC_sA_sC_sG$	71
			~~13B~~ 93	$C_sA_sA_sG_sg_sc_sc_sc_sa_sc_sa_sc_sC_sA_sC_sg$	
			~~13C~~ 94	$C_OA_OA_OG_Og_sc_sc_sc_sa_sc_sa_sc_sC_OA_OC_OG$	
14	136/1	CTACTACAAGTTTATC	~~14A~~ 95 CUR2681	$C_sT_sA_sC_st_sa_sc_sa_sa_sg_st_st_sT_sA_sT_sC$	78
			~~14B~~ 96	$C_sT_sA_sC_st_sa_sc_sa_sa_sg_st_st_sT_sA_sT_sc$	
			~~14C~~ 97	$C_OT_OA_OC_Ot_sa_sc_sa_sa_sg_st_st_sT_OA_OT_OC$	
15	91/1	CAGTCTTGCTCTCGAT	~~15A~~ 98 CUR2682	$C_sA_sG_sT_sc_st_st_sg_sc_st_sc_st_sC_sG_sA_sT$	61
			~~15B~~ 99	$C_sA_sG_sT_sc_st_st_sg_sc_st_sc_st_sC_sG_sA_st$	
			~~15C~~ 100	$C_OA_OG_OT_Oc_st_st_sg_sc_st_sc_st_sC_OG_OA_OT$	
16	262 /1	AAGCAACATCCTGACA	~~16A~~ 101	$A_sA_sG_sC_saacatcctG_sA_sC_sA$	
			~~16B~~ 102	$A_sA_sG_sC_saacatcctG_sA_sC_sa$	

			~~16C~~ 103	$A_OA_OG_OC_O$aacatcctG$_O$A$_O$C$_O$A	
17	1815/4 (intron)	CTCGTCCTTCTCCTCC	~~17A~~ 104 CUR2767	$C_sT_sC_sG_st_sc_sc_st_st_sc_st_sc_sC_sT_sC_sC$	49
			~~17B~~ 105	$C_sT_sC_sG_st_sc_sc_st_st_sc_st_sc_sC_sT_sC_sc$	
			~~17C~~ 106	$C_OT_OC_OG_Ot_sc_sc_st_st_sc_st_sc_sC_OT_OC_OC$	
18	1988/4 (intron)	CATCTTCCTCCAGTCG	~~18A~~ 107 CUR2768	$C_sA_sT_sC_st_st_sc_sc_st_sc_sc_sa_sG_sT_sC_sG$	45
			~~18B~~ 108	$C_sA_sT_sC_st_st_sc_sc_st_sc_sc_sa_sG_sT_sC_sg$	
			~~18C~~ 109	$C_OA_OT_OC_Ot_st_sc_sc_st_sc_sc_sa_sG_OT_OC_OG$	
19	1/1	ACAGAGCTTCAAGACT			
20	17/1	GGATCCAAAGCACCAA			
21	33/1	AAGGACCGATGGAAAT			
22	49/1	TCTGACGAGCGGCTGT			
23	65/1	ATCTTGGCTGCTGGAG			
24	81/1	CTCGATCTGCTTCACC			
25	97/1	GAAAAGCAGTCTTGCT			
26	113/1	GCGTCCAAGGCTT			

		CCT
27	129/1	AAGTTTATCACCT GCA
28	145/1	AGAAGTCAACTAC TAC
29	161/1	CCACACCACGTGG CTG
30	177/1	GATCATTTTGCAA GGC
31	193/1	AATGAAAGAAAG GCTT
32	209/1	TACTTTTCAGAGA GGG
33	225/1	GAATATCACGTTG GAA
34	241/1	CCACATCTACTTC AAG
35	257/1	ACATCCTGACAGT CAT
36	273/1	TTCACACTCTGAA GCA
37	289/1	TTGGCATGCATTT GAC
38	305/1	TTAAAAAACTGGA ATG
39	321/1	CACCTTTTGTCCCT TC
40	337/1	CTCCAGAAAATTC

		ACC
41	353/1	AGCTTTTCCTTATTGG
42	369/1	ATTAATGGTGGCTTCA
43	385/1	ATGATTAGACTAATTC
44	401/1	TTATATTTTCAGAAAC
45	417/1	ATAGCTCAATGGCTGG
46	433/1	AAATTACAAGTTTTAA
47	449/1	TTTTTGTAAATTAAAA
48	465/1	GTCTTCATATTTTATA
49	481/1	TGGCAACTGGGTTTAT
50	497/1	TTTATTGTCACGCAGA
51	513/1	GTGTTAGCATTAATGT
52	529/1	GAGACGGTTTTAAAAA
53	545/1	AAAGCTATTCAGACAT
54	561/1	TTTCACATTTATTT

		TG
55	25/3	CGCTGCTTGCTCTC TC
56	9/3	CCTTTATAAACTG GCA
57	1/3	AACTGGCACGCCC GGC